

What is claimed is:

1. A method of inducing and/or sustaining an immunological CTL response in a mammal, which method comprises:

delivering an antigen in the form of a polypeptide directly to the

lymphatic system of the mammal at a level sufficient to induce an immunologic CTL response in the mammal; and

maintaining the level of the antigen in the mammal's lymphatic system over time sufficient to maintain the immunologic CTL response.

2. The method of claim 1, wherein said antigen is provided as an 8-10 amino acid peptide.

3. The method of claim 1, wherein the peptide sequence is derived from a tumor-associated antigen.

4. The method of claim 3, wherein said tumor-associated antigen is selected from the group consisting of MelanA (MART-I), gp100 (Pmel 17), tyrosinase, TRP-1, TRP-2, MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, p15(58), CEA, RAGE, NY-ESO (LAGE), SCP-1, Hom/Mel-40, PRAME, p53, H-Ras, HER-2/neu, BCR-ABL, E2A-PRL, H4-RET, IGH-IGK, MYL-RAR, Epstein Barr virus antigens, EBNA, human papillomavirus (HPV) antigens E6 and E7, TSP-180, MAGE-4, MAGE-5, MAGE-6, p185erbB2, p180erbB-3, c-met, nm-23H1, PSA, TAG-72-4, CA 19-9, CA 72-4, CAM 17.1, NuMa, K-ras,  $\beta$ -Catenin, CDK4, Mum-1, p16, TAGE, PSMA, PSCA, CT7, telomerase, 43-9F, 5T4, 791Tgp72, alpha-fetoprotein,  $\beta$ -HCG, BCA225, BTAA, CA 125, CA 15-3 (CA 27.29\BCAA), CA 195, CA 242, CA-50, CAM43, CD68\KP1, CO-029, FGF-5, G250, Ga733 (EpCAM), HTgp-175, M344, MA-50, MG7-Ag, MOV18, NB/70K, NY-CO-1, RCAS1, SDCCAG16, TA-90 (Mac-2 binding protein\cyclophilin C-associated protein), TAAL6, TAG72, TLP, and TPS.

5. The method of claim 1, wherein the peptide sequence is derived from a microbial antigen.

6. The method of claim 1, wherein said antigen is provided as a component of a microorganism or mammalian cell.

7. The method of claim 6, wherein said microorganism is a protozoan.

8. The method of claim 6, wherein said microorganism is a bacterium.

9. The method of claim 6, wherein said microorganism is a virus.

10. The method of claim 6, wherein said mammalian cell is an antigen presenting cell.

11. The method of claim 10, wherein said antigen presenting cell is a dendritic cell.

5 12. The method of claim 6, wherein said antigen is a native component of said microorganism or mammalian cell.

13. The method of claim 6, wherein said microorganism or mammalian cell comprises an exogenous antigen.

10 14. The method of claim 6, wherein said microorganism or mammalian cell comprises a recombinant nucleic acid encoding or promoting expression of said antigen.

15 15. The method of claim 13, wherein said microorganism or mammalian cell expresses a tumor-associated antigen.

16. The method of claim 13, wherein said microorganism or mammalian cell expresses a microbial antigen native to a second microbial species.

15 17. The method of claim 13, wherein said antigen is provided as an 8-10 amino acid peptide.

18. A method of inducing and/or sustaining an immunological CTL response in a mammal, which method comprises:

20 delivering an antigen, in the form of a vector comprising a nucleic acid encoding the antigen, directly to the lymphatic system of the mammal at a level sufficient to induce an immunologic CTL response in the mammal; and

maintaining the level of the antigen in the mammal's lymphatic system over time sufficient to maintain the immunologic CTL response.

19. The method of claim 18, wherein the vector comprises a plasmid.

25 20. The method of claim 19, wherein the vector further comprises a bacterium.

21. The method of claim 20, wherein the bacterium is selected from the group consisting of *Listeria*, *Shigella*, *Salmonella*, and *Escherichia*.

22. The method of claim 18, wherein the vector further comprises a virus.

30 23. The method of claim 22, wherein the virus is selected from the group consisting of pox viruses, adenoviruses, adeno-associated viruses, retroviruses, and herpesviruses.

24. The method of claim 18, wherein said nucleic acid encodes a tumor-associated antigen.

25. The method of claim 24, wherein said tumor-associated antigen is selected from the group consisting of MelanA (MART-I), gp100 (Pmel 17), tyrosinase, TRP-1, TRP-2, MAGE-1, MAGE-3, BAGE, GAGE-1, GAGE-2, p15(58), CEA, RAGE, NY-ESO (LAGE), SCP-1, Hom/Mel-40, PRAME, p53, H-Ras, HER-2/neu, BCR-ABL, E2A-PRL, H4-RET, IGH-IGK, MYL-RAR, Epstein Barr virus antigens, EBNA, human papillomavirus (HPV) antigens E6 and E7, TSP-180, MAGE-4, MAGE-5, MAGE-6, p185erbB2, p180erbB-3, c-met, nm-23H1, PSA, TAG-72-4, CA 19-9, CA 72-4, CAM 17.1, NuMa, K-ras,  $\beta$ -Catenin, CDK4, Mum-1, p16, TAGE, PSMA, PSCA, CT7, telomerase, 43-9F, 5T4, 791Tgp72, alpha-fetoprotein,  $\beta$ -HCG, BCA225, BTAA, CA 125, CA 15-3 (CA 27.29\BCAA), CA 195, CA 242, CA-50, CAM43, CD68\KP1, CO-029, FGF-5, G250, Ga733 (EpCAM), HTgp-175, M344, MA-50, MG7-Ag, MOV18, NB/70K, NY-CO-1, RCAS1, SDCCAG16, TA-90 (Mac-2 binding protein\cyclophilin C-associated protein), TAAL6, TAG72, TLP, and TPS.

26. The method of Claim 18, wherein said nucleic acid encodes a microbial antigen.

27. The method of Claim 26, wherein said antigen is a viral antigen.

28. The method of Claim 26, wherein said antigen is a bacterial antigen.

29. The method of Claim 26, wherein said antigen is a protozoal antigen.

30. The method of claim 18, wherein said nucleic acid encodes a protein or other polypeptide.

31. The method of claim 30, wherein said nucleic acid encodes an 8-10 amino acid peptide.

32. The method of claim 18, wherein said nucleic acid is plasmid DNA in a formulation comprising about 1-10% ethyl alcohol, 0-1% benzyl alcohol, 0.25-0.5mM EDTA and a citrate-phosphate buffer of pH 7.4-7.8, comprising about 3-50mM citrate and about 90 -200mM phosphate.

33. The method of claim 32, wherein said formulation comprises 1% ethyl alcohol, 1% benzyl alcohol, 0.5mM EDTA and a citrate-phosphate buffer of pH 7.4 to 7.8 comprising 50mM citrate and 100mM phosphate.

34. A method of inducing and/or sustaining an immunological CTL response in a mammal, which method comprises:

delivering a microorganism or mammalian cell directly to the lymphatic system of the mammal at a level sufficient to induce an immunologic CTL response in the mammal; and

maintaining the level of the microorganism or mammalian cell in the mammal's lymphatic system over time sufficient to maintain the immunologic CTL response.

35. A method of inducing and/or sustaining an immunological CTL response in a mammal, which method comprises:

delivering a nucleic acid capable of conferring antigen expression, directly to the lymphatic system of the mammal at a level sufficient to induce an immunologic CTL response in the mammal; and

maintaining the level of the nucleic acid in the mammal's lymphatic system over time sufficient to maintain the immunologic CTL response.

36. A method of inducing and/or sustaining an immunological CTL response in a mammal, which method comprises:

delivering a non-peptide antigen directly to the lymphatic system of the mammal at a level sufficient to induce an immunologic CTL response in the mammal; and

maintaining the level of the antigen in the mammal's lymphatic system over time sufficient to maintain the immunologic CTL response.

37. An article of manufacture for delivering an antigen that induces a CTL response in an animal, wherein the article is an external device, and which article comprises:

a reservoir of a physiologically-acceptable, antigen-containing composition that is capable of inducing a CTL response in an animal;

a pump connected to the reservoir to deliver the composition at a defined rate;

a transmission line to discharge the composition from the reservoir; and,

a delivery line connected to the transmission line, which delivery line comprises a catheter of at least 20mm for positioning in the animal and for delivery of the composition to the lymphatic system of the animal.

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